Remarks

Claims 38-84 are pending. Claims 38, 45, 46, 49-52, 69, 71, 75, 78, 80, 83-84 have been amended. Claims 43-44, 47-48, 53-64, 67-68, 73-74, 77, and 82 have been canceled. Claim 85 has been added. Support for this added claim can be found in original claim 74. Claims 49-51, 62-64, 72 and 74-84 have been withdrawn from consideration as being drawn to a non-elected invention. As amended, claims 38-42, 45, 46, 49-51 are drawn to a non-elected Group and are presumed withdrawn.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 47 and 60 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Office Action alleges that recitation of "wherein the antibody prevents antigen recognition" is unclear as to which antigen is being recognized by what substance. Applicants have incorporated this limitation into pending claim 38 and canceled claims 47 and 60. As such, the instant rejection is understood to apply only to amended claim 38. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 38 as amended recites "a substance that binds NK-T cells or antigen presenting cells and ... inhibits NK-T cell activation by antigen presenting cells." As such, it is clear that the claim refers to substances such as antibodies that bind NK-T cells or antigen presenting cells in such a manner as to prevent the NK-T cell from binding an antigen presenting cell thereby preventing antigen recognition. It is known in the art and clear from the description that NK-T cells bind antigen presenting cells and are activated thereby via CD1. Specifically, NKT cells

express T-cell Receptors (TCR) (e.g., Vα24-Jα18/Vβ11 in humans) that react with the MHC class I–like molecule CD1 on antigen presenting cells. As such, antibodies to CD1 or Vα24-Jα18 could be used to prevent antigen recognition by the NK-T cell. Applicants note, however, that as amended, claims 38-42, 45, 46, 49-51 are drawn to a non-elected Group from the Restriction Requirement mailed September 11, 2008, i.e., Group I. These claims are therefore presumed withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph

A. Claims 38-48, 52-61, 65-71 were rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Specifically, the Office Action posits that Applicants are not in possession of the generically recited "substance that modulates NK-T cell activity," including a generically recited antibody of undefined specificity (claims 46-48); or a generically recited "substance that modulates IL-13 activity," including a generically recited antibody of undefined specificity (claims 59-60 and 71). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Claim 38 has been amended to recite *inter alia* the limitations of claims 47-48, such that the claim is now limited to substances that bind NK-T cells or antigen presenting cells and either reduce the number of NK-T cells or inhibit the activation of NK-T cells by antigen presenting cells. This amendment is believed to overcome the rejection for claims 38-48. However, as these

claims are now drawn to non-elected subject matter, Applicants presume these claims to be withdrawn and the rejection to be rendered moot.

Claim 52 has been amended such that the claim is now limited to substances that bind to IL-13 and inhibit IL-13 activation of IL-13Rα. The skilled artisan would understand that substances, such as an antibody, that binds IL-13 and inhibits the ability of IL-13 to bind IL-13Rα would be effective in inhibiting IL-13 activation of IL-13Rα. Applicants therefore respectfully request the withdrawal of this rejection. Pursuant to this amendment, claim 74 lacked antecedent basis. As such, claim 74 was canceled and claims 85 was added reciting the limitation of claim 74 as "further comprising" steps. No new matter is added by these new claims.

B. Claims 38-44, 46-48, 52-61, 65-68, 70, 71, and 73 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. Specifically, the Office Action posits that the specification does not enable one of skill in the art to "prevent" an inflammatory response of colitis, except for oxazolone colitis, without undue experimentation. Applicants have amended claims 38 and 52 to delete the phrase "or preventing" and thereby limit the claims to methods of treating. However, Applicants understand by this amendment that the term "treating" covers both treatment of existing symptoms as well as prevention of re-occurrence of symptoms. In other words, the method does not stop being practiced simply because the treatment was successful and the subject's symptoms cease. Continued treatment of the subject to prevent re-occurrence is still considered "treatment" by those of skill in the art.

Rejection Under 35 U.S.C. § 102

A. Claims 38-45, 52-58, and 65-70 were rejected under 35 U.S.C. § 102(e) as being anticipated by Buelow et al. (US Patent No. 6,696,545). Specifically, the Office posits that Buelow et al. teach a peptide for use in inhibiting the production of inflammatory cytokines, such as IL-13, for inhibiting inflammatory response in colitis. Applicants respectfully disagree.

Buelow et al. indicate that the peptides disclosed therein are capable of inhibiting the cellular production of inflammatory cytokines. Buelow et al. proceed to list several exemplary inflammatory cytokines, including IL-12 and IL-13 (column 10, lines 54-57). Buelow et al. then list several inflammatory responses that can be treated using the disclosed peptides, including Crohn's disease and colitis (column 10, lines 63-65). However, there is no indication in Buelow et al. as to which of the cytokines are relevant to each of the listed inflammatory conditions. In the absence of any suggestion as to which cytokine is relevant to which condition, the present combination of IL-13 inhibition and treatment of UC, is neither explicitly disclosed nor enabled by Buelow et al. Moreover, the instant claims are directed to substances that bind to IL-13 and inhibit IL-13 activation of IL-13Rα. Buelow et al. do not teach substances that bind IL-13, such as IL-13 antibodies or IL-13αRa2-Fc, or suggest their use in treating ulcerative colitis. Applicants therefore respectfully request the withdrawal of this rejection.

B. Claims 38-48, 52-61, 65-71 and 73 were rejected under 35 U.S.C. § 102(e) as being anticipated by Heavner et al. (US Pat. Pub. No. 2004/0023337). Specifically, the Office posits that Heavner et al. teach antibodies to mutant forms of IL-13 (e.g., paragraphs 0003 and 0014), and further teach that these can be used for treatment of disease, such as inflammatory bowel disease, ulcerative colitis, and Crohn's disease (e.g., paragraph 0176). According to the Office

Action, antibodies to IL-13 inherently modulate NK-T cell activity, regardless of whether or not this property was known at the time the invention was made. As such, the Office Action alleges that Heavner et al. anticipate the claimed methods. Applicants respectfully disagree.

First, Heavner et al. provide a mutant form of IL-13 (mutein) as well as antibodies generated by this mutein. Heavner et al. do not teach an antibody to IL-13. Rather they teach antibodies to a mutant form of IL-13. Because an antibody to a different protein is expected to have different binding characteristics and functions, no information about the binding of antibodies to mutant IL-13 is relevant to the present invention.

Second, Heavner et al. do not enable treatment of ulcerative colitis, and Crohn's disease. Heavner et al. provided a laundry list of diseases as potential "Mut-IL-13 related diseases," including what appears to be every known "inflammation related disease," "cardiovascular disease," "infectious disease," "malignant disease," and "neurologic disease" (paragraph 0175 to 0180). The Office Action finds it relevant that inflammatory bowel disease, ulcerative colitis, and Crohn's disease were among the hundreds of diseases listed. However, it is unreasonable to suggest that Heavner et al. enabled the treatment of hundreds of diseases merely by providing a comprehensive list of these diseases combined with data that relate only to characterization of antibody binding kinetics. The skilled artisan would no doubt have to engage in undue experimentation to treat any of these diseases based on the guidance (or lack thereof) in the disclosure.

Moreover, even if Heavner et al. had listed only one disease, they were inconsistent in suggesting that that their invention provided a method for modulating or treating Mut-IL-13 related diseases using "at least on antibody or protein of the present invention." This assertion

alone demonstrates a lack of enablement because an antibody generally does not have the same therapeutic effect as its antigen. For example, if the IL-13 mutein activated IL-13 signaling, then an IL-13 antibody would presumably inhibit IL-13 signaling. Moreover, there is no guidance to suggest otherwise. Thus, the skilled artisan would have no way to know which of the mutein and antibody could be used for each of the listed disease. Thus, not only do Heavner et al. boldly suggest that hundreds of diseases can be treated, they also inconsistently propose that it can be done with either the mutein or the antibody. Applicants therefore respectfully request the withdrawal of this rejection.

C. Claims 38-45, 52-58, and 65-70 were rejected under 35 U.S.C. § 102(e) as being anticipated by Cohen et al. (US Pat. Pub. No. 2004/0022787) as evidenced by Heller et al. (Immunity, 2002, 17:629-638). Specifically, the Office Action posits that Cohen et al. teach the use of CTLA4Ig fusion protein for treatment of Crohn's disease and ulcerative colitis (e.g., paragraph 0275). The Office Action then posits that one of skill in the art is aware that CTLA4Ig inhibits activation of CD28 by B7-1 and B7-2 molecules in the course of both normal and pathological immune response. The Office Action further states that Heller et al. provide evidence that activation of CD28 is required for NK-T activation and IL-13 production (e.g., pages 629-630, bridging paragraph). The Office Action then alleges that one of skill in the art would therefore understand that CTLA4Ig is a substance that modulates NK-T cell activity and IL-13 activity, and as such, the teachings anticipate the claimed methods. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended. The pending claims are directed only to the use of substances that bind IL-13 and not generally to any substance that modulates NK-T cell activity. As Cohen et al. do not teach the use of substances

that bind IL-13, such as antibodies to IL-13 or IL-13αRa2-Fc, as claimed, Applicants respectfully request the withdrawal of this rejection.

Conclusions

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

It is believed that no fee is due with this submission. However, the Commissioner is hereby authorized to charge any fees which may be required to Deposit Account No. 14-0629.

Respectfully submitted,

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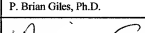
Signature		Date	4/1/09